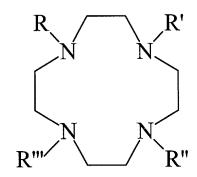
3

4

WHAT IS CLAIMED IS:

- 1. A contrast agent comprising:
- 2 a tetraazacyclododecane ligand having a general formula as 3 follows:



wherein pendent arms R, R', R'' and R''' are amides having a general formula: $-CR_1H-CO-NH-CH_2-R_2$, wherein R_1 includes organic substituents and R_2 is not hydrogen; and

- a paramagnetic metal ion coordinated to said tetraazacyclododecane ligand.
- 2. The contrast agent as recited in Claim 1 further including a water molecule associated with said tetraazacyclododecane ligand and said paramagnetic metal ion such that said water molecule has a $\Delta\omega \bullet \tau_{\rm M} \geq 1$.
- 3. The contrast agent as recited in Claim 2 wherein $2 \qquad \text{said } \Delta \omega \, \geq \, 6 \text{ ppm.}$

- 4. The contrast agent as recited in Claim 2 wherein $2 \qquad \text{said } \tau_\text{M} \, \geq \, 1 \, \, \mu \text{s} \, .$
- 5. The contrast agent as recited in Claim 1 wherein said paramagnetic metal is selected from the group consisting of:

```
3 Eu^{3+};
```

4 Tb^{3+} ;

5 Dy^{3+} ; and

 $6 = \text{Ho}^{3+}$.

6. The contrast agent as recited in Claim 1 wherein said
paramagnetic metal is selected from the group consisting of:

```
Pr<sup>3+</sup>;
```

 $Nd^{3+};$

Sm³⁺;

 Er^{3+} ; and

7 Tm^{3+} .

3 # ##

4 5 4

- 7. The contrast agent as recited in Claim 1 wherein said R_2 does not have a proton exchangeable group.
- 8. The contrast agent as recited in Claim 7 wherein said $R_2 \ \ \text{R}_2 \ \text{is selected from the group consisting of:}$
- 3 Alkyl groups having 20 carbon atoms or less;

Cycloalkyl groups having 20 carbon atoms or less; 4 Alkyloxy groups having 20 carbon atoms or less; 5 Alkyl ethers having 10 oxygen atoms or less and 20 carbon 6 atoms or less; and 7 Polyols having 20 carbon atoms or less. 8 9. The contrast agent as recited in Claim 1 wherein said R_1 is selected from the group consisting of: 1 Η; Alkyl groups having 20 carbon atoms or less; Cycloalkyl groups having 20 carbon atoms or less; Alkyloxy groups having 20 carbon atoms or less; 6 14 Alkyl ethers having 10 oxygen atoms or less and 20 carbon L. 70 atoms or less; and

Polyols having 20 carbon atoms or less.

يَــٰ 9

100

1154

12

13

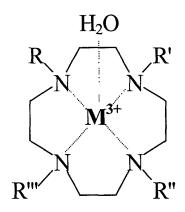
14

2

2

10. A method of using a magnetic resonance (MR) contrast agent, comprising:

subjecting a contrast agent contained within a sample to a radio frequency pulse wherein said contrast agent is a tetraazacyclododecane ligand having a general formula of:



wherein pendent arms R, R', R'' and R''' comprise organic substituents and said tetraazacyclododecane ligand further includes a paramagnetic metal ion (M^{3+}) coordinated to said tetraazacyclododecane ligand and a water molecule (H_2O) associated with said tetraazacyclododecane ligand; and

obtaining a magnetization transfer signal by applying a radio frequency pulse at a resonance frequency of said water molecule.

- 11. The method as recited in Claim 10 wherein said water molecule has a $\Delta\omega \bullet \tau_{\text{M}} \, \geq \, 1 \, .$
 - 12. The method as recited in Claim 10 further includes

- producing a magnetization transfer magnetic resonance image from
 said magnetization transfer signal.
- 13. The method as recited in Claim 10 further includes
 2 applying said radio frequency pulse as a saturating pulse.
- 14. The method as recited in Claim 10 further includes
 2 said contrast agent with at least one pendent arm containing an
 3 ... amide group.
 - 15. The method as recited in Claim 14 wherein said pendent arms are identical and have the general formula: $CHR_1 CO NR_2 R_3, \quad \text{wherein} \quad R_1, \quad R_2 \quad \text{and} \quad R_3 \quad \text{comprise organic}$ substituents.
- 16. The method as recited in Claim 14 wherein said R_1 and R_2 are H, and R_3 has the general formula: $-(CH_2)_nCOOR_4$ where
- n = 1-20; and
- 5 R₄ is selected from the group consisting of:
- 6 H;
- 7 Group IA or IIA metal ions; and
- 8 alkyl groups containing from one to twenty Carbon
- 9 atoms.

្សា 2 ប្រា

3 ≇

4

The state state state states

The method as recited in Claim 14 wherein said paramagnetic metal ion is selected from the group consisting of: 2 Tb^{3+} ; 3 Dy^{3+} ; and Ho^{3+} . 5 The method as recited in Claim 14 wherein said 18. 2 paramagnetic metal ion is selected from the group consisting of: Eu³⁺; Pr^{3+} ; and 5 Ü Nd^{3+} . **L**4 The series The method as recited in Claim 14 wherein said 19. R_1 and R_2 are H, and R_3 has the general formula: -3 $(CH_2)_nP(O)(OR_4OR_5)$ where n = 1-20;said R_4 is selected from the group consisting of: 5 6 Η; 7 alkaline earth metal ions of Groups IA or IIA; and alkyl groups containing one to twenty Carbon atoms; 8 and said R_5 is selected from the group consisting of: 9 Η; 10

11

alkaline earth metal ions of Groups IA or IIA; and

alkyl groups containing one to twenty Carbon atoms.

- 20. The method as recited in Claim 14 wherein said R_1 and R_2 are H, and R_3 has the general formula: $-(CH_2)_nR_4$ where
 - n = 1-20; and

12

3 55

the self was built district of

- R_4 is selected from the group consisting of:
- 5 Pyridine (Py); and
- 6 Phenol (Ph).
 - 21. The method as recited in Claim 14 wherein said pendent arms R and R'' are identical, said pendent arms R' and R''' are identical, and said pendent arms R' and R''' are not equal to said pendent arms R and R'''.
 - 22. The method as recited in Claim 21 wherein said pendent arms R and R'' have the general formula:
- 3 $-CR_1H-CO-NH-CH_2-R_2$; and
- said pendent arms R' and R''' have the general formula:
- 5 $-CHR_3-CO-NH-R_4$ wherein
- said R_1 , R_2 , R_3 , and R_4 comprise organic substituents; and R_2 is not equal to R_4 .
- 23. The method as recited in Claim 14 further includes obtaining said magnetization transfer signal by

- applying a radio frequency pulse at a resonance frequency of
- 4 said protons associated with said amide.

13

2

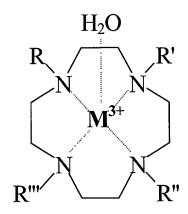
2

2

3

24. A magnetic resonance system, comprising:

a magnetic resonance (MR) contrast agent, wherein said MR agent tetraazacyclododecane ligand, having a general formula of:



wherein pendent arms R, R', R'' and R''' comprise organic substituents and said tetraazacyclododecane ligand further includes a paramagnetic metal ion (M^{3+}) coordinated to said tetraazacyclododecane ligand and a water molecule (H_2O) associated with said tetraazacyclododecane ligand, wherein said MR contrast agent produces a magnetization transfer signal when subjected to a radio frequency pulse; and

a magnetic resonance apparatus configured to produce said frequency pulse.

- 25. The magnetic resonance system recited in Claim 24, further comprising a sample containing said MR contrast agent.
- 26. The magnetic resonance system recited in Claim 24, wherein said sample is a living subject.

2

3

5

2

- The magnetic resonance system recited in Claim 24, produces said magnetic resonance apparatus wherein 2 of said sample from said magnetization transfer image 3 magnetization transfer signal. 4
 - 28. The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of said water molecule.
 - 29. The magnetic resonance system recited in Claim 28, wherein said magnetic resonance apparatus produces a magnetization transfer difference image by applying said radio frequency pulse at a $\Delta \omega$ of said water molecule, acquiring said magnetization transfer signal and subtracting said signal from a MR signal obtained by applying a radio frequency pulse at $-\Delta \omega$.
 - 30. The magnetic resonance system recited in Claim 27, wherein said magnetic resonance apparatus produces said magnetization transfer image by applying said radio frequency pulse at a resonance frequency of protons associated with an amide included in one or more of said pendent arms.

- The magnetic resonance system recited in Claim 24, wherein said radio frequency pulse is produced by said magnetic resonance apparatus and is a saturating pulse. 3
- The magnetic resonance system recited in Claim 24, 32. wherein said saturating pulse is applied at a resonance 2 frequency of said water molecule.

3 01

The Holy Brees

2

- The magnetic resonance system recited in Claim 24, wherein said saturating pulse ranges from about 1 to about 3 seconds.
- The magnetic resonance system recited in Claim 24 34. wherein said water molecule has a $\Delta\omega \bullet \tau_{\text{M}} \geq$ 1.
- 2 The magnetic resonance system recited in Claim 24 35. wherein said $\Delta\omega$ \geq 6 ppm.
- The magnetic resonance system recited in Claim 24 36. wherein said $\tau_{\rm M} \geq 1 \ \mu {\rm s}$. 2